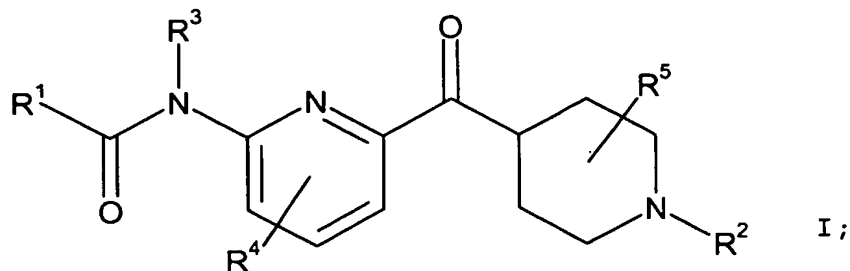


WE CLAIM:

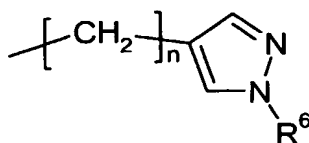
1. A compound of formula I:



or a pharmaceutically acceptable acid addition salt thereof, where;

R<sup>1</sup> is C<sub>1</sub>-C<sub>6</sub> alkyl, substituted C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, substituted C<sub>3</sub>-C<sub>7</sub> cycloalkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl-C<sub>1</sub>-C<sub>3</sub> alkyl, substituted C<sub>3</sub>-C<sub>7</sub> cycloalkyl-C<sub>1</sub>-C<sub>3</sub> alkyl, phenyl, substituted phenyl, heterocycle, or substituted heterocycle;

R<sup>2</sup> is hydrogen, C<sub>1</sub>-C<sub>3</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl-C<sub>1</sub>-C<sub>3</sub> alkyl, or a group of formula



II

II;

R<sup>3</sup> is hydrogen or C<sub>1</sub>-C<sub>3</sub> alkyl;

R<sup>4</sup> is hydrogen, halo, or C<sub>1</sub>-C<sub>3</sub> alkyl;

R<sup>5</sup> is hydrogen or C<sub>1</sub>-C<sub>3</sub> alkyl;

R<sup>6</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl; and

n is an integer from 1 to 6 inclusively.

2. The compound Claim 1 wherein R<sup>5</sup> is hydrogen and R<sup>4</sup> is hydrogen or halogen.

3. The compound of Claim 2 wherein R<sup>4</sup> is hydrogen.

4. The compound of any one of Claims 1 – 3 wherein R<sup>2</sup> is hydrogen or C<sub>1</sub> – C<sub>3</sub> alkyl.

5. The compound of any one of Claims 1 – 4 wherein R<sup>1</sup> is phenyl, substituted phenyl, heterocycle, or substituted heterocycle.

6. The compound of any one of Claims 1 – 5 wherein R<sup>1</sup> is phenyl, substituted phenyl, heterocycle or substituted heterocycle, wherein the heterocycle moiety  
5 is selected from the group consisting of furanyl, thiophenyl, pyrrolyl, pyrrolidinyl, pyridinyl, N-methylpyrrolyl, oxazolyl, isoxazolyl, pyrazolyl, imidazolyl, triazolyl, oxadiazolyl, thiadiazolyl, thiazolyl, thiazolidinyl, N-acetylthiazolidinyl, pyrimidinyl, pyrazinyl, pyridazinyl, isoquinolinyl, benzoxazolyl, benzodioxolyl, benzothiazolyl, quinolinyl, benzofuranyl, benzothiophenyl, and indolyl, and wherein substituted is taken  
10 to mean the ring moiety is substituted with one to three halo substituents; or substituted with one to two substituents independently selected from the group consisting of halo, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, and C<sub>1</sub>-C<sub>4</sub> alkylthio, wherein each alkyl, alkoxy and alkylthio substituent can be further substituted independently with C<sub>1</sub>-C<sub>2</sub> alkoxy or with one to five halo groups each independently selected from fluoro and chloro; or substituted with one  
15 substituent selected from the group consisting of phenyloxy, benzyloxy, phenylthio, benzylthio, and pyrimidinyl, wherein the phenyloxy, benzyloxy, phenylthio, benzylthio, or pyrimidinyl moiety can be further substituted with one to two substituents selected from the group consisting of halo, C<sub>1</sub>-C<sub>2</sub> alkyl, and C<sub>1</sub>-C<sub>2</sub> alkoxy; or substituted with one substituent selected from the group consisting of C<sub>1</sub>-C<sub>4</sub> acyl and C<sub>1</sub>-  
20 C<sub>4</sub> alkoxycarbonyl, and further substituted with zero to one substituent selected from the group consisting of halo, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, and C<sub>1</sub>-C<sub>4</sub> alkylthio.

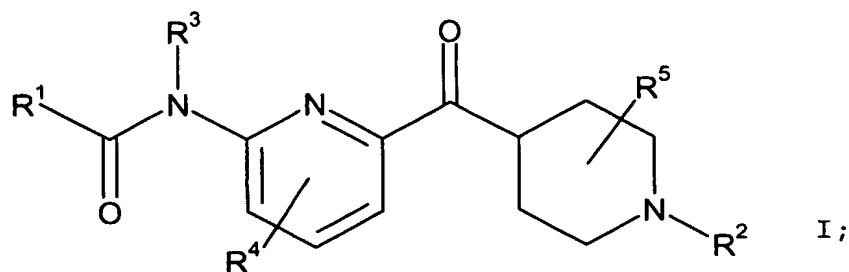
7. The compound of Claim 6 wherein R<sup>1</sup> is phenyl, substituted phenyl, heterocycle or substituted heterocycle, wherein the heterocycle moiety is selected from  
25 the group consisting of pyridinyl, indolyl, benzofuranyl, furanyl, thiophenyl, benzodioxolyl, and thiazolidinyl, and wherein substituted is taken to mean the ring moiety is substituted with one to three halo substituents; or substituted with one to two substituents independently selected from the group consisting of halo, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, and C<sub>1</sub>-C<sub>4</sub> alkylthio, wherein each alkyl, alkoxy and alkylthio substituent can be  
30 further substituted independently with C<sub>1</sub>-C<sub>2</sub> alkoxy or with one to five halo groups each independently selected from fluoro and chloro; or substituted with one substituent selected from the group consisting of phenyloxy, benzyloxy, phenylthio, benzylthio, and pyrimidinyl, wherein the phenyloxy, benzyloxy, phenylthio, benzylthio, or pyrimidinyl moiety can be further substituted with one to two substituents selected

from the group consisting of halo, C<sub>1</sub>-C<sub>2</sub> alkyl, and C<sub>1</sub>-C<sub>2</sub> alkoxy; or substituted with one substituent selected from the group consisting of C<sub>1</sub>-C<sub>4</sub> acyl and C<sub>1</sub>-C<sub>4</sub> alkoxy carbonyl, and further substituted with zero to one substituent selected from the group consisting of halo, C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, and C<sub>1</sub>-C<sub>4</sub> alkylthio.

5

8. A pharmaceutical formulation comprising a compound of any one of Claims 1 - 7 and a pharmaceutical carrier, diluent, or excipient.

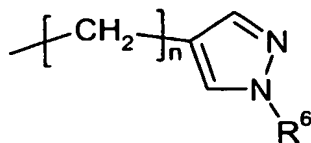
9. A method for activating 5-HT<sub>1F</sub> receptors in a mammal comprising administering to a mammal in need of such activation an effective amount of a compound of formula I:



15 or a pharmaceutically acceptable acid addition salt thereof, where;

R<sup>1</sup> is C<sub>1</sub>-C<sub>6</sub> alkyl, substituted C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, substituted C<sub>3</sub>-C<sub>7</sub> cycloalkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl-C<sub>1</sub>-C<sub>3</sub> alkyl, substituted C<sub>3</sub>-C<sub>7</sub> cycloalkyl-C<sub>1</sub>-C<sub>3</sub> alkyl, phenyl, substituted phenyl, heterocycle, or substituted heterocycle;

R<sup>2</sup> is hydrogen, C<sub>1</sub>-C<sub>3</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl-C<sub>1</sub>-C<sub>3</sub> alkyl, or a group of formula



20 II

II;

R<sup>3</sup> is hydrogen or C<sub>1</sub>-C<sub>3</sub> alkyl;

R<sup>4</sup> is hydrogen, halo, or C<sub>1</sub>-C<sub>3</sub> alkyl;

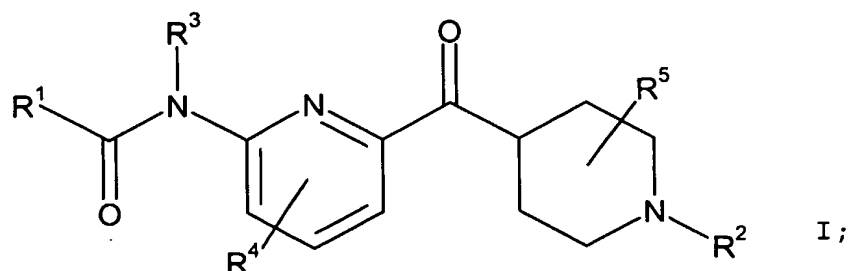
R<sup>5</sup> is hydrogen or C<sub>1</sub>-C<sub>3</sub> alkyl;

25 R<sup>6</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl; and

n is an integer from 1 to 6 inclusively.

10. The method according to Claim 9 wherein the mammal is a human.

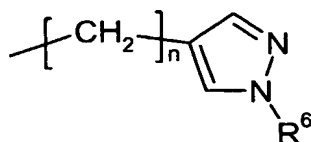
11. A method for inhibiting neuronal protein extravasation in a mammal comprising administering to a mammal in need of such inhibition an effective amount of a compound of formula I:



or a pharmaceutically acceptable acid addition salt thereof, where;

R<sup>1</sup> is C<sub>1</sub>-C<sub>6</sub> alkyl, substituted C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl, substituted C<sub>3</sub>-C<sub>7</sub> cycloalkyl, C<sub>3</sub>-C<sub>7</sub> cycloalkyl-C<sub>1</sub>-C<sub>3</sub> alkyl, substituted C<sub>3</sub>-C<sub>7</sub> cycloalkyl-C<sub>1</sub>-C<sub>3</sub> alkyl, phenyl, substituted phenyl, heterocycle, or substituted heterocycle;

R<sup>2</sup> is hydrogen, C<sub>1</sub>-C<sub>3</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl-C<sub>1</sub>-C<sub>3</sub> alkyl, or a group of formula



II

II;

R<sup>3</sup> is hydrogen or C<sub>1</sub>-C<sub>3</sub> alkyl;

R<sup>4</sup> is hydrogen, halo, or C<sub>1</sub>-C<sub>3</sub> alkyl;

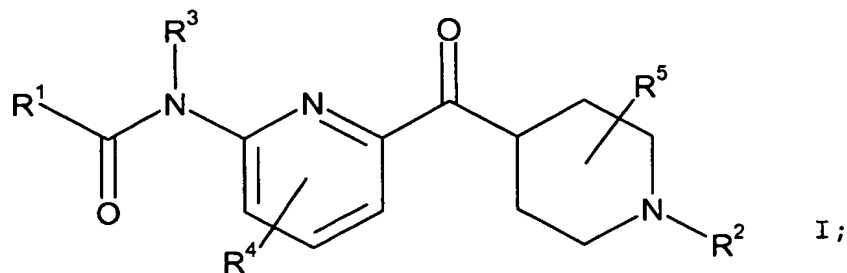
R<sup>5</sup> is hydrogen or C<sub>1</sub>-C<sub>3</sub> alkyl;

R<sup>6</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl; and

n is an integer from 1 to 6 inclusively.

12. The method according to Claim 11 wherein the mammal is a human.

13. A method for the treatment or prevention of migraine in a mammal comprising administering to a mammal in need of such treatment or prevention an effective amount of a compound of formula I:

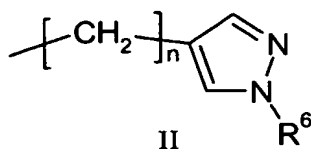


or a pharmaceutically acceptable acid addition salt thereof, where;

$R^1$  is  $C_1$ - $C_6$  alkyl, substituted  $C_1$ - $C_6$  alkyl,  $C_3$ - $C_7$  cycloalkyl, substituted  $C_3$ - $C_7$  cycloalkyl,  $C_3$ - $C_7$  cycloalkyl- $C_1$ - $C_3$  alkyl, substituted  $C_3$ - $C_7$  cycloalkyl- $C_1$ - $C_3$  alkyl, phenyl, substituted phenyl, heterocycle, or substituted heterocycle;

$R^2$  is hydrogen,  $C_1$ - $C_3$  alkyl,  $C_3$ - $C_6$  cycloalkyl- $C_1$ - $C_3$  alkyl, or a group of formula

II



$R^3$  is hydrogen or  $C_1$ - $C_3$  alkyl;

$R^4$  is hydrogen, halo, or  $C_1$ - $C_3$  alkyl;

$R^5$  is hydrogen or  $C_1$ - $C_3$  alkyl;

$R^6$  is hydrogen or  $C_1$ - $C_6$  alkyl; and

$n$  is an integer from 1 to 6 inclusively.

14. The method according to Claim 13 wherein the mammal is a human.

15. A compound according to any one of Claims 1-7 for use as a pharmaceutical.

16. A compound according to any one of Claims 1-7 for use in activating 5-HT<sub>1F</sub> receptors in a mammal.

17. A compound according to any one of Claims 1-7 for use in inhibiting neuronal protein extravasation in a mammal.

5 18. A compound according to any one of Claims 1-7 for use in the treatment or prevention of migraine in a mammal.

19. A compound according to any one of Claims 16-18 wherein the mammal is a human.

10 20. The use of a compound according to any one of Claims 1-7 in the manufacture of a medicament for the activation of 5-HT<sub>1F</sub> receptors in a mammal.

15 21. The use of a compound according to any one of Claims 1-7 in the manufacture of a medicament for the inhibition of neuronal protein extravasation in a mammal.

22. The use of a compound according to any one of Claims 1-7 in the manufacture of a medicament for the treatment or prevention of migraine in a mammal.

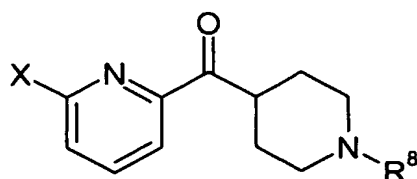
20 23. The use of a compound according to any one of Claims 1-7 in the manufacture of a medicament for the treatment of a disorder associated with dysfunction of the 5-HT<sub>1F</sub> receptors in a mammal.

25 24. The use according to Claim 23 wherein the 5-HT<sub>1F</sub> receptor associated disorder is neuronal protein extravasation.

25 25. The use according to Claim 23 wherein the 5-HT<sub>1F</sub> receptor associated disorder is migraine.

30 26. The use according to any one of Claims 20-25 wherein the mammal is a human.

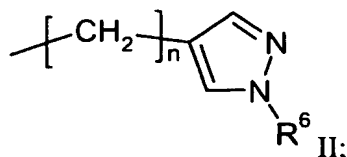
27. A process for preparing a 2-halo-6-(piperidin-4-carbonyl)pyridine compound of formula III



III

where X is bromo or chloro;

$R^8$  is an amino protecting group,  $C_1$ - $C_3$  alkyl,  $C_3$ - $C_6$  cycloalkyl- $C_1$ - $C_3$  alkyl, or a group of formula II



5

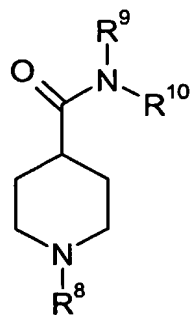
$R^6$  is hydrogen or  $C_1$ - $C_6$  alkyl; and

$n$  is an integer from 1 to 6 inclusively;

comprising

- 1) reacting a 2,6-dihalopyridine selected from 2,6-dibromopyridine and 2,6-dichloropyridine, with *n*-butyl lithium to form 2-halo-6-lithium-pyridine, and then
- 2) reacting the 2-halo-6-lithium-pyridine with a substituted aminocarbonylpiperidine compound of formula IV

10



IV

wherein  $R^9$  and  $R^{10}$  are each methyl, or  $R^9$  and  $R^{10}$ , together with the nitrogen to which they are attached, combine to form azetidiny, pyrrolidinyl, or piperidinyl.

15

28. The process of Claim 27 wherein X is bromo and the 2,6-dihalopyridine is 2,6-dibromopyridine.

20

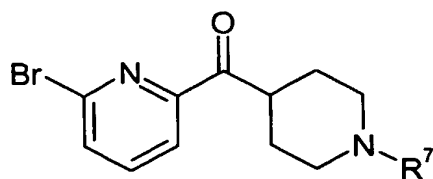
29. The process of either Claim 27 or Claim 28 wherein  $R^9$  and  $R^{10}$  are each methyl.

30. The process of either Claim 27 or Claim 28 wherein R<sup>9</sup> and R<sup>10</sup>, together with the nitrogen to which they are attached, combine to form pyrrolidinyl.

31. The process of any of Claims 27-30 wherein the solvent for step 2) is methyl-*t*-butylether.

32. The process of any of Claims 27-30 wherein the solvent for step 2) is toluene.

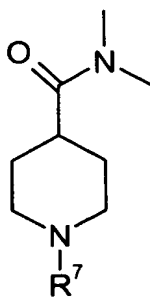
33. A method for preparing a 2-bromo-6-(piperidin-4-carbonyl)pyridine compound of formula III



III

wherein R<sup>7</sup> is C<sub>1</sub>-C<sub>3</sub> n-alkyl, or an amino protecting group;

comprising reacting 2,6-dibromopyridine with *n*-butyl lithium to form 2-bromo-6-lithium-pyridine, and then reacting the 2-bromo-6-lithium-pyridine with a 4-(N,N'-dimethylamino)carbonyl piperidine compound of formula IV



IV

in a methyl-*tert*-butyl ether solvent.